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Critical brain regions for action recognition: lesion symptom mapping in left hemisphere stroke

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A number of conflicting claims have been advanced regarding the role of the left inferior frontal gyrus, inferior parietal lobe and posterior middle temporal gyrus in action recognition, driven in part by an ongoing debate about the capacities of putative mirror systems that match observed and planned actions. We report data from 43 left hemisphere stroke patients in two action recognition tasks in which they heard and saw an action word ('hammering') and selected from two videoclips the one corresponding to the word. In the spatial recognition task, foils contained errors of body posture or movement amplitude/timing. In the semantic recognition task, foils were semantically related (sawing). Participants also performed a comprehension control task requiring matching of the same verbs to objects (hammer). Using regression analyses controlling for both the comprehension control task and lesion volume, we demonstrated that performance in the semantic gesture recognition task was predicted by per cent damage to the posterior temporal lobe, whereas the spatial gesture recognition task was predicted by per cent damage to the inferior parietal lobule. A whole-brain voxel-based lesion symptom-mapping analysis suggested that the semantic and spatial gesture recognition tasks were associated with lesioned voxels in the posterior middle temporal gyrus and inferior parietal lobule, respectively. The posterior middle temporal gyrus appears to serve as a central node in the association of actions and meanings. The inferior parietal lobule, held to be a homologue of the monkey parietal mirror neuron system, is critical for encoding object-related postures and movements, a relatively circumscribed aspect of gesture recognition. The inferior frontal gyrus, on the other hand, was not predictive of performance in any task, suggesting that previous claims regarding its role in action recognition may require refinement.

Introduction

The discovery of mirror neurons in the monkey premotor cortex that fire during both action execution and action observation has fuelled theoretical development in various domains of human social cognition (Rizzolatti and Craighero, 2004; Gallese, 2007; Iacoboni, 2009). In particular, it has been claimed that action understanding in humans is enabled by mirror mechanisms in the inferior frontal gyrus (IFG) and the inferior parietal lobule (IPL), the putative homologue of the monkey mirror system (Rizzolatti and Matelli, 2003; Rizzolatti and Craighero, 2004). On several such accounts, recruitment of mirror neurons in these regions during action observation enables a 'direct matching' between others' gestures and one's own motor system. In support of this account, multiple neuroimaging studies have reported activations in the IFG and IPL—regions involved in action production—when participants observe actions performed by others (e.g. Grafton *et al.*, 1996; Decety *et al.*, 1997; Iacoboni *et al.*, 1999; Buccino *et al.*, 2001, 2004b; Grezes and Decety, 2001; see also Caspers *et al.*, 2010, for a meta-analysis).

The interpretation of such data has recently been challenged, however, on the grounds that activation of mirror-related regions during gesture observation may reflect a simple associative linkage between sensory information and motor plans rather than unitary representations subserving both action production and recognition (Mahon and Caramazza, 2008; Hickok, 2009). Additional support for the direct matching hypothesis may be derived from studies of brain-lesioned patients. Specifically, it may be argued that lesions of IFG and/or IPL disrupting action production and action comprehension in parallel indicate that both are subserved by a common neuroanatomic substrate. On this point, however, neuropsychological findings in patients are ambiguous. On the one hand, gesture production and gesture recognition performance is correlated in large samples of left hemisphere lesioned patients (Buxbaum *et al.*, 2005; Negri *et al.*, 2007; Pazzaglia *et al.*, 2008), consistent with the 'direct matching' hypothesis. On the other hand, double dissociations (i.e. impairment in production but not recognition, and vice versa) have been reported at the single-case level (Halsband *et al.*, 2001; Negri *et al.*, 2007; Tessari *et al.*, 2007; Pazzaglia *et al.*, 2008). In addition, comparison of patient groups with and without action-related deficits (i.e. apraxic and non-apraxic patients) has provided interesting but puzzling results. Impairments in gesture recognition have been associated with damage to the IPL alone in some studies (Buxbaum *et al.*, 2005; Weiss *et al.*, 2008) but with IFG lesions in others (Pazzaglia *et al.*, 2008; Tranel *et al.*, 2008). Recently, Fazio *et al.* (2009) revived the debate by showing that IFG-lesioned aphasic patients without apraxic symptoms were unable to order action pictures in the correct temporal sequence.

The failure of group comparison studies to provide a clear answer to the question of whether mirror regions are necessary for action recognition is at least in part attributable to methodological issues (Fazio *et al.*, 2009; Hickok, 2009). The difficulties arise from (i) the absence of consensus on the criteria used to characterize patients as apraxic, (ii) small sample sizes, and (iii) sometimes subtle but often important differences in the characteristics of the tasks used to evaluate gesture recognition performance. This latter concern is particularly relevant in studies investigating the role of the IFG in gesture recognition, as this region is well known to be involved in a range of language and executive processes (Price, 2000; Badre and Wagner, 2007; Grodzinsky and Santi, 2008). In aphasic patients, the comprehension of actions correlates with linguistic deficits (Saygin *et al.*, 2004). Moreover, the IFG has been shown to support action recognition in tasks that require overt naming of action displays (Tranel *et al.*, 2008). Even in the absence of verbal output requirements, many of the tasks used to assess action recognition have required response selection (e.g. deciding the correctness of a gesture performed by an actor), placing demands on the executive system (Pazzaglia *et al.*, 2008). Consideration of such general task requirements tempers the conclusion that action recognition relies on 'direct matching' mediated by a putative mirror neuron system.

In addition to the IFG and IPL, numerous neuroimaging studies have reported activation of the posterior middle temporal gyrus (MTG) when subjects passively observe actions (Caspers *et al.*, 2010). Such data, in the context of the posterior MTG's localization adjacent to visual area MT, which appears to encode human movement (Beauchamp and Martin, 2007), have prompted the suggestion that the posterior MTG is a component of a broad visuo-motor mirror neuron system (see Noppeney, 2008, for review) despite the fact that it does not contain motor mirror neurons in the monkey (Rizzolatti and Craighero, 2004). However, the observation of posterior MTG activation does not address the question of whether the posterior MTG is critical for gesture recognition; it is here that lesion data are invaluable.

In the present study, we consider the performance of 43 patients with left brain damage in two gesture recognition tasks and a control task with highly similar linguistic requirements. Contrary to other studies (Buxbaum *et al.*, 2005; Pazzaglia *et al.*, 2008; Fazio *et al.*, 2009), patients were not classified along behavioural/anatomical dimensions. Instead, the relationship between lesions of the IFG, the IPL, and the posterior temporal lobe and performance in the three tasks was assessed using regression-based lesion analyses. Whole-brain voxel-based lesion symptom mapping (VLSM) analysis was also performed to confirm the results of the regression analyses, and to further ensure that no additional clusters of voxels outside of the regions of interest played a crucial role in gesture recognition.

Based on a number of previous studies with apraxic patients (Heilman *et al.*, 1982; Buxbaum *et al.*, 2005; Weiss *et al.*, 2008), we predicted that posterior (IPL, posterior temporal lobe) but not anterior (IFG) regions would be critically involved in the recognition of action.

Material and methods

Subjects

Forty-three patients with left-hemisphere stroke (28 males and 15 females) participated in the study. All patients had cortical lesions. Subjects were recruited from the Neuro-Cognitive Rehabilitation

Research Registry at the Moss Rehabilitation Research Institute (Schwartz *et al*., 2005). Patients were excluded if database records indicated language comprehension deficits of sufficient severity to preclude comprehension of task instructions. Subjects over the age of 80 years and/or with histories of co-morbid neurologic disorders, alcohol or drug abuse or psychosis were also excluded. All patients gave informed consent to participate in the behavioural testing in accordance with the guidelines of the institutional review board of the Albert Einstein Healthcare Network and were paid for their participation. Thirty-nine patients also provided informed consent to participate in

an MRI or CT imaging protocol at the University of Pennsylvania School of Medicine. Subjects were paid for their participation and reimbursed for travel expenses. Demographic data are reported in Table 1.

Behavioural tasks

All participants performed three forced-choice-matching tasks involving the same 24 action verbs that refer to transitive actions (see Supplementary material for a complete list).

Table 1 Demographic data and behavioral scores on the spatial gesture recognition task (Spatial rec), the semantic gesture recognition task (Semantic rec) and the verbal comprehension control task (Verbal comp)

Patient	Gender	Age	Handedness	Education	Lesion volume	Spatial rec	Semantic rec	Verbal comp
1	M	62	R	13	14 871	91.67	91.70	96.43
2	M	47	R	16	148 831	79.17	79.17	92.90
3	F	45	R	16	95 940	75.00	87.50	92.90
4	F	48	R	12	52 518	91.67	91.67	100.00
5	M	40	R	11	50 976	83.33	100.00	96.40
6	M	57	L	12	269 930	75.00	91.67	92.86
7	M	71	R	08	17 800	66.67	66.67	67.86
8	M	57	R	13	43 876	75.00	95.83	100.00
9	M	67	R	12	231 754	62.50	70.83	75.00
10	M	51	R	11	32 695	79.17	91.67	96.43
11	M	74	R	08	43 852	66.67	95.83	92.86
12	F	40	R	13	137 337	87.50	100.00	96.43
13	M	60	R	13	186 244	83.33	83.33	78.60
14	M	58	R	11	101 058	50.80	62.50	92.86
15	M	54	R	18	266 061	75.00	79.17	92.86
16	M	44	R	11	48 292	83.33	83.33	89.29
17	F	47	R	16	150 768	91.67	95.83	96.42
18	M	73	R	12	16 038	83.33	95.83	100.00
19	F	48	L	12	77 262	70.83	66.67	89.29
20	M	61	R	16	54 080	79.17	83.33	89.30
21	F	59	R	12	28 765	75.00	95.83	92.90
22	F	53	R	12	60 596	75.00	87.50	89.29
23	M	41	R	14	76 184	91.67	95.83	96.43
24	F	53	R	16	307 942	58.33	62.50	78.57
25	F	71	R	14	82 977	75.00	95.83	96.43
26	M	53	R	18	51 603	87.50	95.83	100.00
27	M	58	R	12	71 169	62.50	70.83	75.00
28	M	66	R	12	110 241	91.67	100.00	96.43
29	F	48	R	12	27 695	95.83	100.00	100.00
30	M	59	L	16	143 394	95.83	95.83	100.00
31	M	69	R	09	77 326	87.50	87.50	100.00
32	M	62	R	12	86 546	100.00	87.50	96.43
33	F	61	R	12	5407	83.33	91.67	100.00
34	M	58	R	12	9255	87.50	95.83	100.00
35	M	55	R	10	28 517	91.67	95.83	95.83
36	F	47	L	14	173 600	54.16	79.17	85.71
37	M	57	R	15	57 976	75.00	87.50	100.00
38	F	58	R	15	37 025	100.00	83.33	100.00
39	F	52	R	16	227 624	54.17	75.00	78.57
40	M	47	R	14	186 422	100.00	100.00	96.43
41	M	62	R	14	84 923	79.17	87.50	92.86
42	F	70	R	12	17 856	70.83	83.33	92.86
43	M	52	L	19	243 226	79.17	79.17	89.28

rec = recognition; comp = comprehension.

Semantic and spatial gesture recognition tasks

Following Buxbaum *et al.* (2005), two forced-choice gesture recognition tasks were conducted. Both required selecting the action (from a choice of two) that matched a spoken and written verb. In the semantic recognition task, participants heard an action verb repeated twice (e.g. 'Sawing . . . Sawing.'), and simultaneously viewed the verb visible on a 3" × 5" card on the tabletop for the duration of the trial. After a 2 s pause, they heard the letter 'A' spoken aloud and then saw two repetitions of a videotaped examiner performing a gesture. After an additional 2 s pause, they heard the letter 'B' spoken, followed by two repetitions of a second gesture. One gesture of each pair was the correct match to the verb (e.g. sawing), and the other was incorrect by virtue of a semantic relationship to the target gesture (e.g. hammering). Semantic foils were chosen for their categorical semantic relationships with targets, e.g. sawing/hammering (both tool-related actions), combing hair/brushing teeth (both grooming actions), carving meat/peeling (both food preparation actions); however, semantic distance within each category was not controlled. Order of the target and foil within the trial was randomized. On each trial, the subject selected the correct gesture by verbalizing or pointing to the appropriate letter ('A' or 'B') displayed on a piece of paper on the table; there were no time constraints for responding. There were 24 semantic trials.

In the spatial recognition task, methods were identical except that the foil was incorrect by virtue of an error in the hand posture, arm posture or amplitude/timing components. There were 24 spatial trials, 8 each with hand posture, arm posture and amplitude/timing foils [this task was used in a previous study (Buxbaum *et al.*, 2005), in which we showed that apraxic patients are particularly deficient in detecting errors in the hand posture component of observed actions. In this study, there proved to be insufficient statistical power to detect differences in the neural representation of these specific components of observed action; therefore, they will not be further discussed]. For example, the foil for the 'sawing' trial consisted of a correctly bent arm position and characteristic forward and back arm movement with an incorrect 'clawed', splay-fingered hand posture (i.e. a hand posture foil).

Verb comprehension control task

The verb comprehension control task was designed to assess patients' comprehension of the specific action verbs used in the study, without requiring access to gesture knowledge. Moreover, the format of this control task was highly similar to that of the gesture recognition tasks (i.e. forced choice matching of a visual stimulus to a target verb).

In each trial, participants heard and viewed an action verb (as above) and three pictures of manipulable objects taken from the Snodgrass and Vanderwart corpus (Snodgrass and Vanderwart, 1980). They were asked to point to the object picture that matched the verb (e.g. hammering–hammer).

Imaging methods

Structural images were acquired using MRI ($n = 23$) or CT ($n = 20$). Twenty-two patients were scanned on a 3 T Siemens Trio scanner. High-resolution whole-brain T_1-weighted images were acquired (repetition time = 1620 ms, echo time = 3.87 ms, field of view = 192 × 256 mm, 1 × 1 × 1 mm voxels) using a Siemens 8-channel head coil. In accordance with established safety guidelines (MRI safety; www.mrisafety.com), one patient was scanned on a 1.5 T Siemens Sonata because of contraindication for a 3 T environment. For this patient, whole-brain T_1-weighted images were acquired (repetition time = 3000 ms, echo time = 3.54, field of view = 24 cm) with a slice thickness of 1 mm using a standard radio-frequency head coil. As MRI was contraindicated for the remaining 20 patients, they underwent whole-brain CT scans without contrast (60 axial slices, 3–5 mm slice thickness) on a 64-slice Siemens SOMATOM Sensation scanner.

Lesion segmentation and warping to template

For seven of the patients with high-resolution MRI scans available electronically, lesions were segmented manually on a 1 × 1 × 1 mm T_1-weighted structural image. The structural scans were registered to a common template using a symmetric diffeomorphic registration algorithm (Avants *et al.*, 2006; see also http://www.picsl.upenn.edu/ANTS/). This same mapping was then applied to the lesion maps. To optimize the automated registration, volumes were first registered to an intermediate template constructed from images acquired on the same scanner. A single mapping from this intermediate template to the Montreal Neurological Institute space 'Colin27' volume (Holmes *et al.*, 1998) was used to complete the mapping from subject space to Montreal Neurological Institute space. The final lesion map was quantized to produce a 0/1 map, 0 corresponding to a preserved voxel and 1 corresponding to a lesioned voxel. A voxel was considered lesioned when > 50% of the voxel volume was affected. After being warped to Montreal Neurological Institute space, the manually drawn depictions of the lesions were inspected by H.B.C., an experienced neurologist who was naive with respect to the behavioural data. For the other 36 patients, H.B.C. used MRICro (http://www.cabiatl.com/mricro/mricro/index.html) to draw lesion maps directly onto the Colin27 volume, after rotating (pitch only) the template to approximate the slice plane of the patient's scan. The individual lesions were visually inspected and analogue areas marked as lesioned on the template. Excellent intra- and inter-rater reliability has been previously demonstrated with this method (Schnur *et al.*, 2009). An illustration of the 43 lesion drawings is presented in Fig. 1.

Lesion-symptom analysis

Using regression analyses, we assessed the degree to which damage to our three regions of interest, namely Brodmann area (BA) 44/45 (hereafter, IFG for brevity), BA 39/40 (hereafter, IPL) and BA 21/22/37 (hereafter, posterior temporal lobe), predicted behavioural scores. For each patient, the total lesion volume and percentage damage were computed using the MRIcron image analysis program (www.mricro.com/mricron). Lesions were overlaid on the Brodmann cytoarchitectonic map provided by the MRIcron program and a count of the number of voxels damaged within each BA was performed. Percent damage to ventral premotor regions of the IFG was calculated by summing the voxels lesioned in BA 44 and BA 45 and representing them as a fraction of the total voxels in BAs 44 and 45. Similar analyses were performed to calculate percent damage to the IPL (BAs 39 and 40) on the one hand, and to the posterior temporal lobe (BAs 21, 22 and 37) on the other. The BAs that composed our three regions of interest showed > 10% damage in at least 30% of patients. A stepwise regression analysis was conducted on each of the
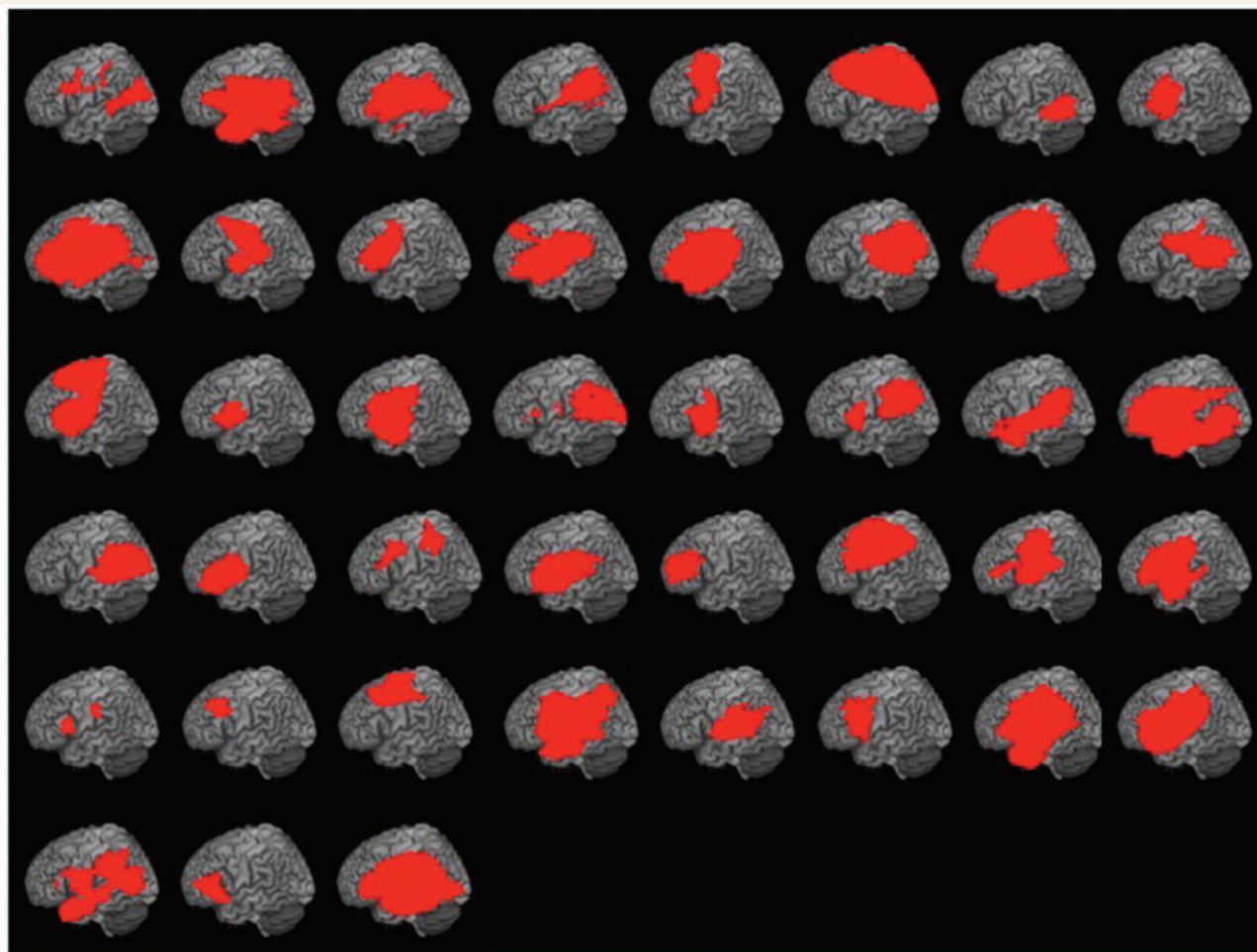
Figure 1 Illustration of the 43 left hemisphere lesions displayed on a template brain. Lesions are represented on the surface of the brain but display both cortical and subcortical damage.

gesture recognition scores, with overall lesion volume, performance in the comprehension control task, and percentage damage to IFG, IPL and posterior temporal lobe as predictors.

Additionally, for the purpose of visualization and to ensure that no additional voxels were critically involved in the recognition tasks outside of the regions of interest, we used the non-parametric mapping method implemented as part of the MRIcron analysis package (http://www.sph.sc.edu/comd/rorden/mricron/stats.html) to carry out a whole-brain VLSM analysis of the voxels most associated with (i) semantic recognition scores, (ii) spatial recognition scores and (iii) verb comprehension scores. After excluding voxels in which fewer than five participants had a lesion, the number of voxels qualifying for analysis was 318 350, or 43% of the 738 535 voxels in the left hemisphere (using counts from the electronic automated anatomical labelling atlas) (Tzourio-Mazoyer et al., 2002). At each voxel, a pairwise comparison (t-test, converted into Z-scores) was performed to assess for differences between scores of participants with and without damage at that voxel. The statistical analysis was thresholded at several levels. The false discovery rate correction was used as a strict control of Type I error. However, we also assessed results at more lenient thresholds to avoid Type II errors, in particular in the IFG.

Moreover, since the false discovery rate correction is less stringent with decreasing numbers of voxels tested, we also corroborated any negative results of the VLSM analyses (e.g. in the IFG) at the region of

interest level using the VoxBo brain-imaging package (www.voxbo .org). As in the whole-brain VLSM analyses, a t-test was performed in each voxel for which at least five patients had a lesion. However, by restricting the voxels tested to the same regions of interest as the ones we considered in the regression analyses, namely BA 44/45 (20 888 voxels), BA 39/40 (27 129 voxels) and BA 21/22/37 (37 628 voxels), we reduced the false discovery rate correction used to compute a statistical threshold at each voxel. In this way, we could be certain of the reliability of any negative results in the whole-brain VLSM analysis.

Results

Behavioural scores

Individual scores for these three behavioural tasks are presented in Table 1. Participants' mean performance was 92% correct (SD = 9%) in the verb comprehension task, 87% correct (SD = 11%) in the semantic recognition task and 80% correct (SD = 13%) in the spatial recognition task. All between-task differences in accuracy were significant (P < 0.001).

Lesion-symptom mapping results

Region of interest-regression analyses

A stepwise regression analysis was conducted on each of the gesture recognition scores, with overall lesion volume, performance in the comprehension control task and percentage damage to a given region of interest as predictors (IFG, IPL and posterior temporal lobe; see the 'Material and methods' section).

Although the overall lesion volume was moderately correlated with the behavioural tasks ($r = -0.40$ for the verb comprehension task and $r = -0.30$ for the gesture recognition tasks), when considered in concert with performance in the comprehension control task and percentage damage to IFG, IPL, and posterior temporal lobe, lesion volume proved not to be a significant independent predictor of behavioural task performance in any of the region of interest regression models tested and will not be further discussed.

The regression analysis on the semantic recognition scores indicated that the comprehension control task significantly predicted gesture recognition performance ($r = 0.734$, $P < 0.001$). More importantly, it revealed that the posterior temporal lobe (BAs 21, 22 and 37) was an independent predictor of semantic recognition scores above and beyond the comprehension control task (partial correlation $r = -0.341$, $P < 0.05$). However, neither lesions to the IFG (BAs 44 and 45) nor IPL (BAs 39 and 40) contributed to the fit of the model (IFG: partial correlation $r = -0.058$, $P = 0.72$; IPL: $r = -0.073$, $P = 0.65$).

The regression analysis on the spatial recognition scores showed that the comprehension control task significantly predicted gesture recognition performance ($r = 0.648$, $P < 0.001$). Importantly, damage to the IPL ($r = -0.328$, $P < 0.05$), but not the IFG (partial correlation $r = 0.095$, $P = 0.55$) or posterior temporal lobe (partial correlation $r = -0.138$, $P = 0.39$), improved the fit of the predictive model.

The results of the voxel-based analyses are displayed in Figs 2 and 3. In VLSM, differences in power between regions are due to differences in the frequency with which lesions impinge the region. Figure 2 shows a colour map of the number of patients with lesions in each voxel and suggests the relative (not absolute) power of each voxel for detecting an association, if one exists, between lesion status and the behavioural measures. The map shows good coverage of the regions of interest and indicates a frequency of $n > 20$ lesions in the peri-sylvian regions, including the IFG.

Figure 3 presents statistical maps of the Z-scores of voxels associated with the three behavioural tasks. Note that the Z-value observed in each individual voxel is independent of the level at which the VLSM analysis (whole-brain or region of interest) is conducted. The number of voxels included in the analysis determines which Z-value reaches the false discovery rate-corrected threshold. Importantly, as will be discussed next, we observed the same patterns of results using the whole brain and region of interest approaches.

Whole-brain VLSM analyses

For the semantic gesture recognition task (Fig. 3A), a large region of high Z-scores was observed in the temporal cortex. In particular, a cluster of 9344 voxels in the posterior MTG exceeded the statistical threshold corrected for multiple comparisons (region in bright yellow, Z-scores > 2.87, $q > 0.05$ false discovery rate corrected). There was also a large cluster of 4487 voxels with high Z-scores more anterior in the middle and inferior temporal gyrus (Z-scores > 2.58, $P < 0.005$ uncorrected). An additional region with high Z-scores was seen in the middle frontal gyrus (voxel count = 255 for Z-scores > 2.58, $P < 0.005$ uncorrected). Critically, there were no Z-scores in the IFG that exceeded even relaxed, uncorrected thresholds.

For the spatial gesture recognition task (Fig. 3B), no voxels reached the false discovery rate statistical threshold corrected for multiple comparisons. However, it is important to note that a large cluster of 916 voxels in the IPL partly bordering the intraparietal sulcus was associated with the highest Z-scores (Z-scores > 2.58, $P < 0.005$ uncorrected). This is consistent with the results obtained in the regression analysis described above. A large region of the MTG, both posterior and more anterior (voxel count = 8109 for Z-scores > 2.58, $P < 0.005$ uncorrected), as well as a small portion of the middle frontal gyrus was also observed with similar Z-scores. Importantly, there were again no Z-scores in the IFG that surpassed even an uncorrected threshold of $P < 0.05$.
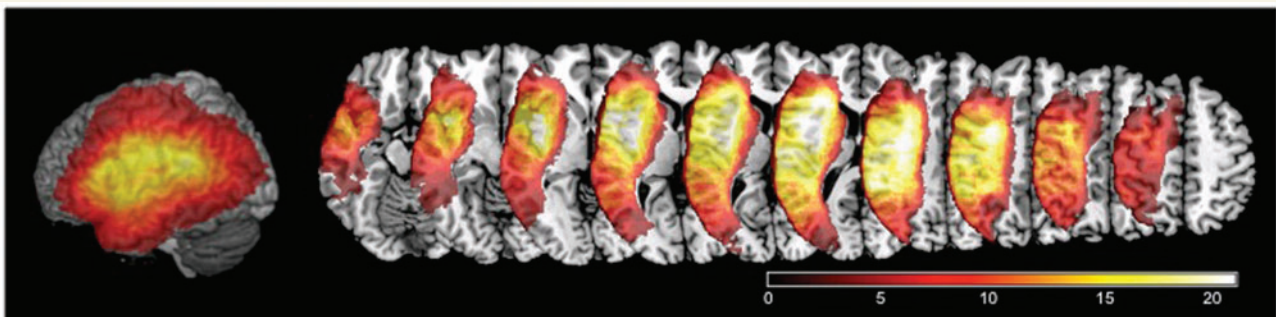

Figure 2 Map depicting lesion overlap of the 43 subjects in the left hemisphere. Only voxels lesioned in at least five subjects were included. The regions rendered in bright red correspond to an overlap of 5–10 patients. The regions rendered in orange correspond to an overlap of 10–15 patients. The regions of maximum overlap rendered in the lightest colours (yellow and white) are lesioned in more than one-third of the patients (overlap of ≥15) and are situated in the peri-sylvian regions.
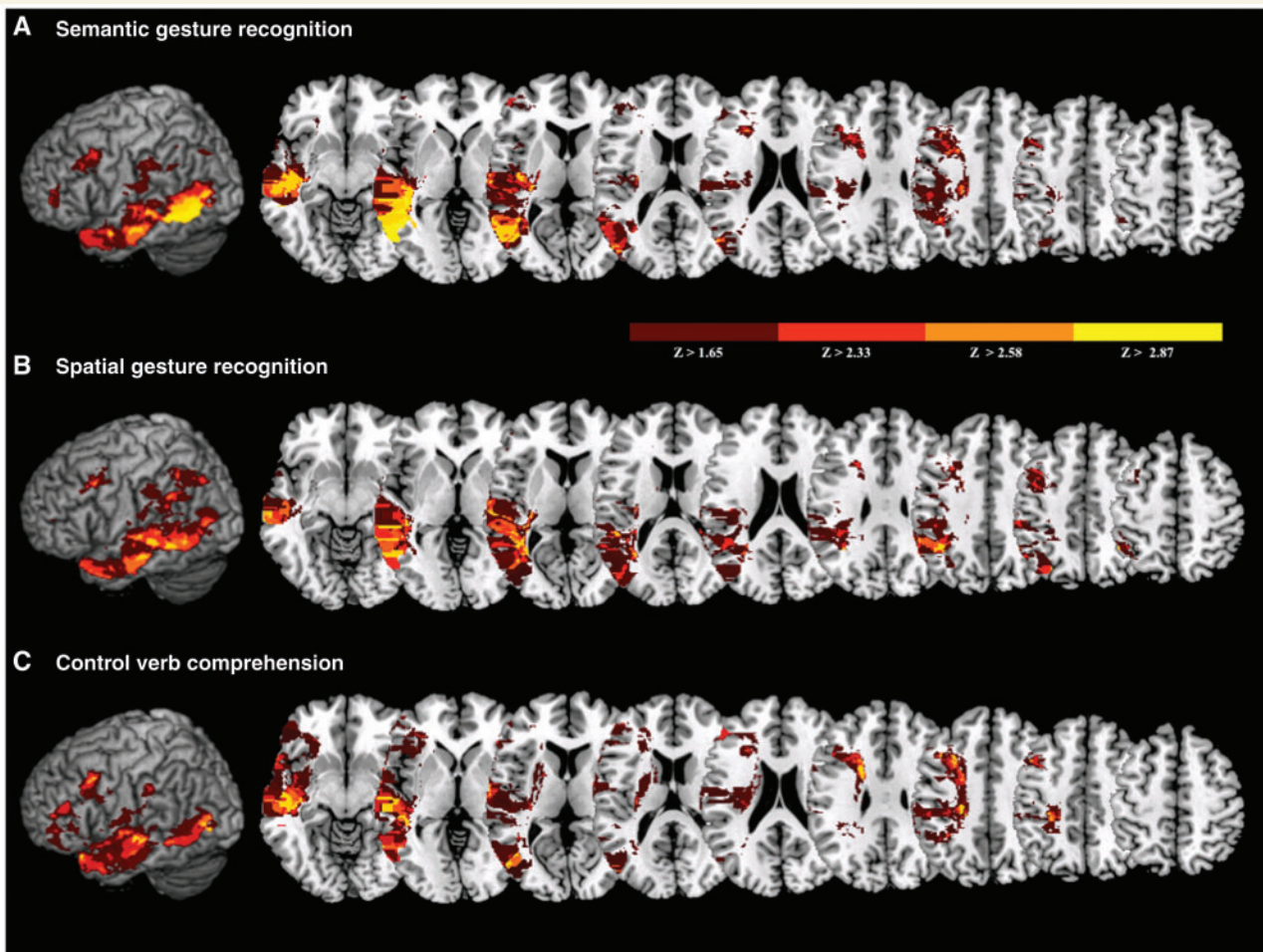
Figure 3 Maps of the reliability (Z-scores) of the difference in semantic recognition scores (**A**), spatial recognition scores (**B**), and verb comprehension scores (**C**) between patients with and without lesions in each voxel (rendered on the Montreal Neurological Institute–space ch2bet volume). Voxels rendered in dark red, light red, and orange correspond to Z-scores > 1.65 (P < 0.05 uncorrected), Z-scores > 2.33 (P < 0.01 uncorrected), and Z-scores > 2.58 (P < 0.005 uncorrected), respectively. Voxels displayed in bright yellow were associated with Z-scores > 2.87 that reached the false discovery rate-corrected threshold at P < 0.05 in the whole-brain analysis on the semantic gesture recognition scores.

Finally, for the verb comprehension control task (Fig. 3C), the highest Z-scores associated with an uncorrected threshold at P < 0.005 were evident in the temporal lobe (voxel count = 5044 for Z-scores > 2.58). Small clusters in the middle frontal gyrus (voxel count = 299 for Z-scores > 2.58) and in the IFG (voxel count = 385 for Z-scores > 2.58) also reached this threshold.

Region of interest-VLSM analyses

To further ensure that the absence of significant voxels in the IFG associated with the gesture recognition tasks was not due to an overly conservative correction for multiple comparisons, we ran complementary VLSM analyses in each region of interest (i.e. IFG, IPL, and posterior temporal lobe). Despite a less stringent false discovery rate correction in the region of interest-VLSM analyses, no voxels in the IFG or IPL were significantly associated with the gesture recognition tasks, and no IFG voxels reached even uncorrected thresholds, as can be seen in Fig. 3. In accordance with the whole-brain analysis, a few significant voxels were evident in the IFG in the verb comprehension control task (voxel

count = 86, Z-scores > 2.90, P < 0.05 false discovery rate corrected). In the IPL, the region of interest–VLSM analysis revealed, consistent with the regression analyses, that the highest Z-scores (P > 0.005 uncorrected) were associated with the spatial gesture recognition task. As expected, given the more lenient threshold, the involvement of the temporal lobe (BA 21/22/37) was again observed in all three tasks (voxel count = 28 732, 22 942 and 15 495 significant voxels for the semantic gesture recognition task, the spatial gesture recognition task and the verb comprehension control task, respectively).

Discussion

We investigated the hypothesis that gesture recognition—that is, the ability to identify a gesture with a semantically meaningful label—depends upon posterior brain structures in the temporal and parietal lobes and is not critically dependent on the IFG. This hypothesis has implications for accounts positing that gesture

recognition relies upon a putative mirror neuron system in the ventral premotor cortex. We assessed the performance of 43 left-hemisphere stroke patients in two verb-gesture matching tasks (semantic and spatial gesture recognition) and a control verb–object matching task (verb comprehension). Regression and VLSM analyses revealed a parallel pattern of results that are inconsistent with a critical role for human mirror systems in action recognition.

Despite a large sample size and a pattern of lesion distribution that robustly represented the IFG (maximal lesion counts of 32 in this region), there was no evidence that the IFG made a contribution to performance of either gesture recognition task. It has been noted that there is considerable anatomical variability in the frontal lobes (Brett *et al.*, 2002); it might be argued that this, in combination with the use of a normalization procedure, may render the detection of an IFG contribution more difficult. While this possibility cannot be ruled out, we failed to detect involvement of the IFG even when we considered percent damage to relatively large regions (BAs) and used relaxed statistical thresholds. We believe it is unlikely that neuroanatomic variability explains the complete absence of evidence for IFG involvement.

Consistent with our predictions, two posterior regions proved critical for gesture recognition. The semantic gesture recognition task relies on the integrity of the posterior temporal lobe (BAs 21, 22, and 37). In addition, performance in the spatial but not in the semantic recognition task is disrupted by lesions to the IPL (BA 39/40). These data suggest that the role of 'mirror areas' in action recognition requires reconsideration, as will be discussed below.

Two additional regions were identified in the whole-brain analyses in all three behavioural tasks, namely the anterior part of the temporal lobe and the middle frontal gyrus. In previous functional neuroimaging and lesion studies, involvement of these regions has not been specific to gesture recognition but seems rather to be related to more general processes at play when accessing the meaning of an action verb. Indeed, damage to the left anterior temporal lobe has been associated with semantic errors in aphasic patients, indicating that this region plays a role in word-concept mapping (Schwartz *et al.*, 2009). Among other more general executive functions, the middle frontal gyrus has been related to action naming (Johnson-Frey, 2004). Nevertheless, its role is not restricted to gesture knowledge, and this region has been implicated in tasks that require access to functional knowledge regarding objects (Bach *et al.*; Goldenberg and Spatt, 2009). The present finding of common anterior temporal and middle frontal involvement in all tasks is consistent with the proposal that such semantic and executive processes are likely to be at play in the control task as well as the gesture recognition tasks. We now turn to discussion of the data as they address specifically the neural substrates of gesture recognition.

The IFG is not critical for gesture recognition

In several recent accounts (Gallese *et al.*, 1996; Rizzolatti *et al.*, 1996; Hamzei *et al.*, 2003; Buccino *et al.*, 2004*a*; Rizzolatti and Craighero, 2004; Binkofski and Buccino, 2006; Iacoboni and Mazziotta, 2007; Kilner *et al.*, 2009), Broca's area (BAs 44/45)

is a core component of the mirror neuron system involved in human action understanding. The present findings challenge this interpretation and suggest that prior findings of IFG involvement may be a function of incidental characteristics of the tasks used to assess gesture recognition.

One possibility is that the IFG involvement previously observed in action recognition tasks reflects domain-general cognitive control processes, such as those required to perform difficult response selection (Thompson-Schill *et al.*, 1997; Rajah *et al.*, 2008; Goghari and MacDonald, 2009). In support of this possibility, Pazzaglia *et al.* (2008) asked participants, including 33 left hemisphere stroke patients, to watch a video depicting a transitive or intransitive gesture and decide whether the gesture was correct or not. Incorrect transitive gestures were movements performed with an incorrect tool, whereas incorrect intransitive gestures contained erroneous spatial hand or finger configurations. Using VLSM, the investigators found that transitive and intransitive gesture discriminations were exclusively associated with voxels in the IFG. In the present study, subjects performed at a higher level of accuracy [Mean 86% correct in comparison with 68% correct in the Pazzaglia *et al.* (2008) study], and there was no evidence for IFG involvement. One possibility is that the patients in the study of Pazzaglia *et al.* (2008) were more severely impaired overall. It remains possible, however, that the observed IFG involvement in that study was related to task difficulty.

A second possible reason for the previously observed IFG involvement in action recognition is that the IFG mediates complex syntactic processing of event sequences of many types, including but not limited to action stimuli (Fadiga *et al.*, 2009). Recent data from Fazio *et al.* (2009) support this view. Aphasics with IFG lesions were more impaired than controls in ordering pictures of simple human actions (e.g. grabbing a bottle, turning one's head and pointing) but not pictures of physical events (e.g. door closing) (note that the simple actions presented in the human action condition differ quite markedly from the transitive and intransitive actions classically used in the gesture recognition literature, e.g. tooth brushing, hitch-hiking). The deficit in sequencing simple human actions was correlated with the sequencing of linguistic materials (sentence segments and word syllables). Despite these 'syntactic' deficits, however, it is noteworthy that Fazio *et al.* (2009, p. 1986) report that the 'patients' understanding of the global meaning of the observed actions was mostly preserved'.

These findings corroborate those from a functional MRI study by Schubotz and von Cramon (2002), demonstrating activation of the IFG during the prediction of sequential patterns, irrespective of the type of stimuli (visual or auditory). Interestingly, prediction of size (visual sequences) recruited premotor areas involved in hand movements, while the prediction of pitch (auditory sequences) activated Broca's area. This suggests that abstract sequences of perceptual stimuli, and not only observed actions, are mapped onto a representation in the IFG. Although it is plausible that this sequencing capacity might derive from a largely evolved mirror neuron system (Fadiga *et al.*, 2009), the data do not compel the interpretation that the IFG mirror area is critical for action understanding. The absence of IFG involvement in the present study is explicable on the assumption that the gesture recognition tasks we used (matching a pantomime to a verb) placed less

stress on prediction or syntactic abilities than the tasks used by Fazio *et al.* (2009) and Schubotz and von Cramon (2002).

This interpretation of the variable role of the IFG as a function of task demands is consistent with its proposed role in a putative hierarchy of cognitive control (Koechlin *et al.*, 2003; Badre, 2008). Compelling evidence indicates that the IFG supports higher-order control of behaviour, including the selection of motor representations in response to external contextual cues. Action recognition tasks may rely on the integrity of the IFG to the degree that they place a heavy burden on such selection demands in addition to their requirements for gesture recognition.

There are a number of additional possible reasons for the differences between the findings of Fazio *et al.* (2009), Pazzaglia *et al.* (2008) and the present study. For example, the lesion analyses of Pazzaglia *et al.* (2008) considered transitive and intransitive gestures as an aggregate, the former requiring semantic discrimination and the latter requiring spatial discrimination. It is conceivable that as a result, there was reduced power to detect lesions (e.g. in the parietal lobe) related to deficits in either type of discrimination alone, along with increased power to detect meta-task capacities (such as executive function). Finally, the Pazzaglia task—to judge the 'correctness' of an action—could arguably be accomplished based on recognition of the familiarity of a structural description of the action without the necessity of contacting full action meaning. Similar arguments have been made in the case of patients who are able to judge whether stimuli are real objects or not but nevertheless are unable to name them or match them to their names (Warrington and Taylor, 1978; for a review see Warrington, 2009). Thus, the semantic network may not need to be contacted in the 'correctness judgement' task. The main point is that in the absence of a detailed task analysis, it is possible to generate conclusions that are overly broad. In fact, considering all of the relevant studies together, we conclude that the IFG may play a role in circumscribed aspects of action processing, without being necessary for or central to the overall recognition of action.

The IPL supports the spatiotemporal coding of gestures

The regression results indicated that the IPL significantly predicted performance in the spatial recognition task, even after controlling for overall lesion volume and verb comprehension. These results are consistent with the whole-brain VLSM and region of interest–VLSM analyses, where the highest observed Z-scores were associated with IPL voxels, although in the latter cases they failed to reach the statistical threshold corrected for multiple comparisons. A probable reason for this disparity in significance is that the VLSM approach requires that precisely the same voxels are damaged in a significant proportion of participants, whereas the regression approach takes into account only proportion damage to the entire region of interest. Thus, as compared with the regression approach, the VLSM approach loses in statistical power what it gains in spatial resolution, especially in the less-covered regions, an important reason for the complementarity of the two methods. Taken together, these data suggest that while we may be

confident that the IPL is involved in spatial gesture recognition, more precise localization within the IPL must await further investigation.

Another potential objection to the claim that the IPL mediates the spatial aspects of action recognition is that the apparent IPL involvement may be an artefact of the greater difficulty of the spatial recognition task as compared with the other tasks. However, results of the regression analysis indicate that even when two independent measures of severity are taken into account (lesion volume and scores in the comprehension control task), damage to the IPL still significantly predicts spatial gesture recognition. Thus, our findings indicate that the IPL is critical in coding the posture of the effectors and the amplitude and timing of the movement in action recognition. However, the IPL does not appear to support the identification of the correct gesture for a particular object.

These data are consistent with previous observations of specific spatiotemporal gesture production deficits in patients with IPL damage. Apraxia is usually assessed with gesture imitation tasks and frequently diagnosed in relation to an abnormal number of spatiotemporal errors during the reproduction of gestures performed by a model (Haaland and Flaherty, 1984; Haaland *et al.*, 2000; Buxbaum *et al.*, 2005, 2007). As in our spatial recognition task, spatial and temporal errors in production concern the posture of the different effectors (arm, hand, fingers) and the characteristics of the movement such as amplitude and timing. Patients with IPL lesions make more spatial errors during imitation of pantomimes than other kinds of errors such as parapraxic errors (i.e. correct gesture that is not appropriate for the target object, e.g. brushing nails with toothbrush) or using the body part as an object (Halsband *et al.*, 2001). Moreover, the influence of parietal lesions on imitation is frequently more pronounced for meaningless than meaningful gestures (Kolb and Milner, 1981; Goldenberg and Hagmann, 1997; Haaland *et al.*, 2000; Weiss *et al.*, 2001; Tessari *et al.*, 2007) and affect in particular the position of the hand when reproducing the gesture (Haaland *et al.*, 2000; Buxbaum *et al.*, 2005, 2007; Goldenberg and Karnath, 2006). In a previous study, we demonstrated that parietal-lesioned apraxics were specifically impaired in both reproducing and recognizing the correct hand posture required to perform transitive movements (Buxbaum *et al.*, 2005). In the light of neuropsychological studies on imitation, the present findings suggest that the IPL is critical for both action imitation and recognition; however, its decisive role is restricted to the processing of spatiotemporal gestural information, particularly for object-related actions (see Goldenberg, 2009, for a review). If mirror mechanisms exist within the IPL, such mechanisms may be crucial for encoding and retrieving the coordinates of transitive movements in time and space. However, as will be discussed next, additional neural mechanisms mediated by other cortical regions are required to access gesture meaning.

The posterior temporal cortex integrates visuo-motor and object knowledge to derive action meaning

Results of regression and VLSM analyses both showed that the posterior temporal lobe is critical in accessing the meaning of an

action, i.e. in retrieving and identifying the correct object-related gesture. In the regression analyses, temporal lobe BAs reached significance only in the semantic recognition task. In parallel, in the VLSM analyses, despite evidence of temporal lobe involvement in all three behavioural tasks, a large cluster of voxels in the posterior MTG reached the corrected statistical threshold only in the semantic gesture recognition task (region in bright yellow in Fig. 3A). As behavioural performance was significantly better in the semantic than in the spatial recognition task, the posterior temporal lobe findings do not reflect task difficulty.

The posterior MTG is frequently activated in functional neuroimaging studies of action observation (see Caspers *et al.*, 2010, for a meta-analysis) and has been highlighted in numerous neuroimaging studies on action semantics and tool concepts (see Martin, 2007; Noppeney, 2008 for reviews), acting together with the fronto-parietal motor circuit. The posterior MTG is activated when participants name tool versus animal stimuli (see Chouinard and Goodale, 2009, for a meta-analysis), retrieve conceptual information about manipulable objects (e.g. Kellenbach *et al.*, 2003; Tranel *et al.*, 2003; Boronat *et al.*, 2005), process action versus object concepts (e.g. Kable *et al.*, 2005; Assmus *et al.*, 2007) and after learning the use of novel objects (e.g. Kiefer *et al.*, 2007; Weisberg *et al.*, 2007). Indeed, the present results suggest that the posterior temporal lobe (and not the IFG or IPL) supports the understanding of action meaning. This raises the question of the exact role of the posterior MTG in action-related activities, and its interaction with the visuo-motor mirror system.

Several authors have suggested that the posterior MTG may play a crucial role in multimodal integration and/or supramodal representation of tool-related actions (Kable *et al.*, 2005; Beauchamp and Martin, 2007; Binder *et al.*, 2009; Willems *et al.*, 2009), thus serving as a cornerstone of the tool knowledge system. In particular, because of its physical proximity to area MT and its connections with the IPL, the posterior MTG may be responsible for integrating motion features of tool-related gestures with other types of object-related semantic information (Beauchamp and Martin, 2007).

Consistent with this possibility, Willems *et al.* (2009) showed, in a functional MRI study, that the posterior MTG, but not the IFG, was selectively activated for the matching of action verbs and pantomimes. These findings corroborate those observed in our gesture recognition task and indicate that the posterior MTG is particularly involved in the comprehension of action verb–pantomime associations. Similar findings are reported by Xu *et al.* (2009), who demonstrated in a functional MRI study that the posterior MTG was the largest common area of activation for processing symbolic gestures and spoken language. They suggest that the posterior MTG may represent a supramodal node for a domain-general semiotic system in which meaning is paired with symbols, irrespective of the modality (spoken words, gestures, images, sounds, etc.). The hypothesis that the posterior MTG serves as a supramodal semantic node is further supported by numerous recent investigations of semantic processing (Lau *et al.*, 2008; Binder *et al.*, 2009).

A complementary interpretation of the integrative role of the posterior MTG in action recognition can be derived from recent propositions regarding a subdivision of the dorsal stream that supports 'vision for action' (Milner and Goodale, 1995). We (Buxbaum, 2001) and others (Rizzolatti and Matelli, 2003; Johnson-Frey, 2004; Pisella *et al.*, 2006; Vingerhoets *et al.*, 2009) have proposed that the dorsal stream is subdivided into two neuroanatomically and functionally distinct systems. Rizzolatti and Matelli (2003), in particular, characterized these systems in the monkey as the dorso-dorsal and ventro-dorsal streams. Based on studies of neuronal pathway interconnectivity, they suggested that the ventro-dorsal stream includes area MT and portions of the IPL, and projects to portions of the IFG. We have proposed that in humans, the dorso-dorsal stream supports real-time, on-line actions based on object structure and involves bilateral superior fronto-parietal regions. In contrast, the dorso-ventral system is a left-lateralized system comprising the left IPL and portions of the posterior temporal lobe and ventral premotor cortex and is specialized for skilled object-related actions. The ventro-dorsal system represents the core features of object use actions and articulates action and object knowledge.

The existence of a distinct 'functional manipulation' system has received compelling evidence in recent years (see Buxbaum and Kalenine, 2010, for a review). However, the precise neuroanatomic substrates of such a system in the human brain remain unclear. Accounts of the posterior MTG emphasizing its multi-modal role in integrating gestural with other semantic information are consistent with the role frequently accorded to the ventro-dorsal stream. In this context, the present results suggest that current models of the functional-manipulation system in humans should be expanded to include the posterior MTG. Specifically, we suggest that the left IPL and posterior MTG form a closely associated functional network, wherein the IPL encodes the spatiomotor aspects of object-related gestures, and the posterior MTG plays a critical role in interpretation of meaning.

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Supplementary material

Supplementary material is available at *Brain* online.

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